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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/565,673	08/10/90	VAN DER LAAN J	

HM12/0329
DEBRA J. GLAISTER PATENT AGENT
GENENCOR INTERNATIONAL INC.
925 PAGE MILL ROAD
PALO ALTO CA 94304

EXAMINER	
FRONDA,C	
ART UNIT	PAPER NUMBER
1652	61

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No. 07/565,673	Applicant(s) Van Der Lann et al.
	Examiner Christian L. Fronda	Group Art Unit 1652

☒ Responsive to communication(s) filed on *December 15, 2000 (paper no. 60)*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *41-53* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *41-53* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. In the **AMENDMENT** dated December 10, 2000 (paper no.60), Applicants have amended claims 44 and 49.

2. Claims 41-53 are under consideration in this Office Action.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 41-53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 41, 49, and 50 are directed toward a gene encoding all possible "mutant high alkaline" proteases and all possible "wild-type high alkaline" proteases. The specification, however, only provides the following representative species of mutant alkaline proteases encompassed by these claims: gene encoding a mutant alkaline protease comprising a nucleotide sequence consisting of the gene encoding the wild-type alkaline protease of *Bacillus* novo species PB92 having the codon for M216 replaced with a codon coding for Q, the codon for S160 replaced with a codon coding for D, or the codon of N212 replaced with a codon coding for D. Furthermore, the specification only teaches the wild-type alkaline protease of *Bacillus* novo species PB92 as the single representative species of the claimed "wild-type high alkaline" proteases. There is no disclosure of any particular structure to function/activity relationship in the disclosed species. The specification also fails to describe additional representative species of these "mutant high alkaline" proteases or "wild-type high alkaline" proteases by any identifying structural characteristics or properties for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms

that a skilled artisan would recognize Applicants were in possession of the claimed invention. Claims 42-47 which depend from claims 41 are also rejected because they do not correct the defect of claim 41. Claim 49 which depends from claim 48 is also rejected because it does not correct the defect of claim 49. Claims 51-53 which depend from claim 50 are also rejected because they do not correct the defect of claim 50.

5. Claims 41-53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the wild-type alkaline protease of *Bacillus* novo species PB92, the gene encoding said wild-type alkaline protease of *Bacillus* novo species PB92, and a gene encoding a mutant alkaline protease comprising a nucleotide sequence consisting of the gene encoding the wild-type alkaline protease of *Bacillus* novo species PB92 having the codon for M216 replaced with a codon coding for Q, the codon for S160 replaced with a codon coding for D, or the codon of N212 replaced with a codon coding for D; does not reasonably provide enablement for any wild-type alkaline protease or any gene encoding any mutant alkaline protease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of claims 41, 49, and 50 encompass any wild-type alkaline proteases or any genes encoding any mutant alkaline proteases. The specification provides guidance and examples for the wild-type alkaline protease of *Bacillus* novo species PB92 and a gene encoding a mutant alkaline protease comprising a nucleotide sequence consisting of the gene encoding the wild-type alkaline protease of *Bacillus* novo species PB92 having the codon for M216 replaced with a codon coding for Q, the codon for S160 replaced with a codon coding for D, or the codon of N212 replaced with a codon coding for D. While molecular biological techniques and genetic manipulation to make the claimed enzyme and gene are known in the prior art and the skill of the artisan are well developed, knowledge regarding the specific source and type of wild-type alkaline protease and the specific mutation in the claimed gene encoding the mutant alkaline protease is lacking. Thus, searching for the specific wild-type alkaline protease and the specific mutation in the claimed gene encoding the mutant alkaline protease is well outside the realm of routine experimentation and predictability in the art of success is extremely low.

The amount of experimentation to determine the specific wild-type alkaline protease and the specific mutation in the claimed gene encoding the mutant alkaline protease is enormous.

Such experimentation entails screening a vast number of organisms for an organism containing a wild-type alkaline protease, selecting and isolating a wild-type alkaline protease from the selected biological source, obtaining the amino acid sequence of the isolated wild-type alkaline protease, obtaining the gene encoding the isolated wild-type alkaline protease from libraries constructed from the selected biological source, and recombinantly expressing the wild-type protease using the gene encoding the wild-type protease. Furthermore, such experimentation entails selecting a wild-type alkaline protease to mutate, selecting a mutation to perform on the amino acid sequence of the wild-type alkaline protease such as substitution, addition, deletion, or combinations thereof of amino acid residues, obtaining the gene encoding the selected wild-type alkaline protease, mutate the gene encoding the wild-type alkaline protease, express the mutant alkaline protease, and screening for mutants that still have alkaline protease activity.

Since routine experimentation in the art does not include screening a vast number of biological sources for a specific type of wild-type alkaline protease and making and screening for mutant alkaline proteases where the expectation of obtaining a desired wild-type alkaline protease or making a mutant alkaline protease is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the specific wild-type alkaline protease and the specific type of mutation in the claimed gene encoding a mutant alkaline protease. Without such a guidance, the experimentation left to those skilled in the art is undue.

Claims 42-47 which depend from claims 41 are also rejected because they do not correct the defect of claim 41. Claim 49 which depends from claim 48 is also rejected because it does not correct the defect of claim 49. Claims 51-53 which depend from claim 50 are also rejected because they do not correct the defect of claim 50.

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 41-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 41 is indefinite because it is not known what is the specific mutation of the claimed "mutant high alkaline protease". Furthermore, the meaning of the phrase "high alkaline" is not known since "high" is a relative term and it is not known at what pH range is considered to be "high alkaline". Claims 42-47 which depend from claim 41 are also rejected because they do not correct the defect of claim 41.

Claims 48 is indefinite because the meaning of the phrase "high alkaline" is not known since "high" is a relative term and it is not known at what pH range is considered to be "high alkaline". Claim 49 which depends from claim 48 is also rejected because it does not correct the defect of claim 49.

Claim 50 is indefinite because the meaning of the phrase "high alkaline" is not known since "high" is a relative term and it is not known at what pH range is considered to be "high alkaline". Claims 51-53 which depend from claim 50 are also rejected because they do not correct the defect of claim 50.

Conclusion

8. No claim is allowed.

9. Claims drawn to a method for producing a mutant alkaline protease comprising expressing in a mutant alkalophilc *Bacillus* host, a mutant alkaline protease encoded by a polynucleotide comprising a nucleotide sequence which has the codon for M216, S160, or N212 of the gene encoding the wild-type alkaline protease of *Bacillus* novo species PB92 replaced with another codon encoding another amino acid, wherein said mutant alkalophilic *Bacillus* host comprises a chromosomal deletion of the gene encoding the wild-type alkaline protease of *Bacillus* novo species PB92, may overcome the stated rejections.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L. Fronda whose telephone number is (703)305-1252. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703)308-3804. The fax phone number for this Group is (703)308-0294. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703)308-0196.

CLF

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NASHAAT T. NASHED PHD.
PRIMARY EXAMINER